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ORIGINAL ARTICLES

METHYLENE BLUE IN CYANIDE AND CARBON MONOXIDE POISONING—A SURVEY OF THE LITERATURE*

By HARRY B. LUKE, M.D.

In July, 1932, three men were taken to the Park Emergency Hospital in San Francisco. Fifteen minutes previously they had collapsed after drinking a beverage later found to contain large amounts of cyanide, in the office of one of the three. The condition on admission was recognized as probably cyanide poisoning and treatment was started at once, but all three of the men died, despite gastric lavage, artificial respiration and the administration of cardiac and respiratory stimulants. This experience led J. C. Geiger,[1] the U. S. Public Health Surgeon who was director of the hospital, to reflect on the inadequacies of the treatment of cyanide poisoning. As a result he went to pharmacologists Hanzlik of Stanford University and C. D. Leake of the University of California and asked if they could suggest an antidote for cyanide poisoning.

At that time Hanzlik[2] was demonstrating in his pharmacology lectures how methylene blue stimulated the respiration of laboratory animals when it had been diminished by the administration of cyanide. So he suggested to Geiger that methylene blue might be tried as an antidote for cyanide poisoning in human beings. In fact some of his students had asked if it could not be used. These experiments with methylene blue were the outgrowth of earlier observations.

In 1926 Sahlin[3] had demonstrated that methylene blue stimulated respiration when it was depressed by sodium cyanide, and enabled an animal to survive an otherwise fatal dose of cyanide. In 1930 Eddy[4] of the University of Michigan supported this observation, and in 1931[5] showed that the effects of a fatal intravenous dose of cyanide were reduced, and the animal survived, if 10 mgm. of methylene blue per kilo of body weight were given intravenously 10 minutes before the cyanide was given or not over 2 minutes after the poison was given. M. M. Brooks[6&7] reported similar results.

The mechanism by which cyanide kills had been demonstrated by O. W. Warburg[8] in 1928. It inhibits the oxidizing ferment of the tissues throughout the body, thereby abolishing its ability to use oxygen.

Knowing that cyanide killed by destroying the oxidizing ferments, and having experimentally observed that methylene blue protected animals from fatal doses of cyanide, the conclusion of these earlier investigators was that methylene blue acted as an oxidative ferment in place of the one destroyed by the cyanide. In other words, they felt that methylene blue acted as a respiratory enzyme or stimulant in place of the one destroyed by the cyanide.

So when Geiger, of the Public Health Service, asked Hanzlik and Leake for an antidote for cyanide poisoning, they replied that there was experimental evidence that methylene blue was that antidote and recommended the intravenous administration of 50 cc. of 1% autoclaved solution of methylene blue.

Geiger then equipped himself with his remedy and waited patiently for a chance to use it. In September 1932 another man entered the Park Emergency Hospital. He had swallowed a dose of cyanide, instantly regretted his rash act and told his friends. He was promptly taken to the hospital where he was comatose on admission. His respiration was slow and regular; his pupils were contracted and sluggish; his lips were a bright vermilion color and his breath had a peculiar odor, suggesting paraldehyde or chloral. He had spasm of his voluntary muscles with moderate opisthotonos and extreme hyperextension of his hands and feet. He was given a gastric lavage with soda bicarbonate solution at once. Within 5 minutes of his entry he was given intravenously 50 cc. of 1% solution of methylene blue which Geiger had waiting for him. Five minutes later the man became conscious, followed by a chill and a complete clinical recovery within 15 minutes. This patient had taken 1 gm. of potassium cyanide, 0.05 gm. was recovered from

*Presented at the Internes Conference May 10, 1934, at the Charles V. Chapin Hospital, Providence, R. I.

the stomach washings, and the rest, about 0.95 gm., was probably absorbed.

Since then Geiger[9] has reported two more cases of cyanide poisoning treated with methylene blue. The first of these took two #0 capsules of potassium cyanide. 0.05 gm. was recovered from stomach washings and 1.1 gm. absorbed. This patient received 50 cc. of methylene blue followed by momentary recovery and then a return to unconsciousness. So a second 50 cc. of methylene blue was given a half hour after the first dose and followed by recovery.

The second patient took 6.5 gm. of potassium cyanide by mouth and was given two 50 cc. doses of methylene blue one-half hour apart. Both of these patients recovered without other treatment. Furthermore, no untoward symptoms from the administration of 100 cc. of 1% methylene blue (1 gm.) were observed.

No other reports of cases treated with methylene blue have been made to date.

Geiger now had three cases of cyanide poisoning successfully treated with methylene blue. Clearly the drug had successfully stimulated the respiration in cyanide poisoning; why not try it in carbon monoxide poisoning which also caused a respiratory death? Accordingly Geiger[10] treated a couple of cases of carbon monoxide poisoning with intravenous methylene blue. The first one had been unconscious for half an hour and had been given artificial respiration with oxygen and carbon dioxide administration with improvement in respiration and cyanosis, but had not yet returned to consciousness. He was given 50 cc. of 1% methylene blue with little change in his condition. The carbon dioxide and oxygen administration was continued. After another hour the dose of methylene blue was repeated and the patient roused sufficiently to talk coherently for a moment, then relapsed into unconsciousness. In a half an hour 20 cc. more of the dye was given with renewed response and eventual recovery. The second case was given the 50 cc. of the dye soon after he became unconscious. In two minutes he was talking coherently. Geiger concluded his report by stating that the dye, in carbon monoxide poisoning, as in cyanide poisoning, acted on the oxidation-reduction processes of the bodily tissues and resulted in a stimulation of the respiratory and circulatory centers.

At this time M. M. Brooks[11] supplied animal experiments which showed that methylene blue was an antidote for carbon monoxide poisoning. Rabbits were allowed to breathe carbon monoxide until respiration ceased. Artificial respiration was then given to all of them, and half received intravenous methylene blue. 90% of the rabbits receiving the dye recovered while only 20% of the controls did so.

Several other clinicians[12,13,14] then reported a case or two apiece of carbon monoxide poisoning treated with methylene blue, in addition to oxygen and carbon dioxide administration.

It now appeared as if we had been given a valuable and almost specific method of treating cyanide and carbon monoxide poisoning. But these earlier reports were next to be investigated by other men.

The mechanism by which cyanide causes death was demonstrated by Warburg.[8] To repeat, it inactivates the oxidizing ferments of the tissues, thereby abolishing the ability of the body tissues to use oxygen.

How does methylene blue protect the organism from cyanide poisoning? Does it replace the enzyme destroyed by the cyanide, and of itself act as an oxidizing ferment to the tissues, as Hanzlick, Geiger and other earlier investigators supposed, or does it act by some other mechanism?

Methylene blue had long been known to convert hemoglobin into methemoglobin. Compemale[15] had proved that this took place in vivo as early as 1891. Wendel,[15] Wendel and Schaffer,[17] and Warburg, Kubowitz and Christian[18] showed that this also occurred in vitro. The latter group of men also showed that methemoglobin reacted with hydrocyanic acid to form an unusually stable compound, cyanmethemoglobin. So stable is this compound that the cyanide radicle could not be removed in the presence of a vacuum. They showed in vitro that methemoglobin was an effective reagent for absorbing hydrocyanic acid from exceedingly dilute solution or gases. Then they demonstrated that in vivo the injection of methylene blue and the formation of methemoglobin leads to the fixation of cyanide as cyanmethemoglobin within the blood cell. This occurred whether the cyanide entered the blood stream by absorption from the lungs, from the alimentary tract or from tissues where the cyanide has penetrated before the methylene blue was injected.

Methylene blue thus acts through a definite antidotal mechanism on cyanide. What of the supposition that it replaces the function of the tissue oxi-

dizing ferment destroyed by cyanide. The only experimental basis for this supposition is furnished by Warburg, quoted by Haggard and Greenberg,[22] who showed that methylene blue, applied to isolated tissue, counteracted the influence of cyanide or the tissue ferment. This was found to hold true only for isolated bloodless tissue, a condition not present in the poisoned animal. Hence there is no experimental basis for the assumption that methylene blue acts as an enzyme to tissue oxidation reactions. Recently Hanzlik and Richardson[23] again suggest that methylene blue seems to stimulate external respiration, and Haggard and Greenberg[22] observe that the animal's respirations are momentarily increased in depth and force after the injection of methylene blue. This is most likely a momentary reaction to the intravenous injection of the dye. In any event, it seems conclusively demonstrated that the chief antidotal action of the dye is produced through the production of methemoglobin and the formation of the very stable cyanmethemoglobin, fixing the cyanide within the red cell.

Since methylene blue acts by forming methemoglobin, Wendel[19] reasoned that the injection of methemoglobin alone should give protection against cyanide. Furthermore, any substance which formed methemoglobin more rapidly than methylene blue should be more effective than the dye. Amyl nitrite also forms methemoglobin when exposed to red cells. So Wendel took 20 cc. of blood per kilogram of body weight from dogs, converted the hemoglobin to methemoglobin with amyl nitrite (removing any excess of the latter) and reinjected the cells into the dogs. The dogs were then injected with a lethal dose of hydrocyanic acid (about 6 mg. per kilogram) and were found to be completely protected. Furthermore, a similar volume of methemoglobin cells, when injected into dogs approaching death from a lethal dose of hydrocyanic acid, rapidly revived the animals.

Hug,[20] the professor of Pharmacology of the Faculty of Medicine of Rosario, states that there are three groups of substances capable of acting on cyanides. These are:

1. Substances containing sulphur—such as sodium thiosulphate, sodium tetrathyocyanate, glutathionate and cystine.

2. Derivatives of sugars—such as dioxyacetone and triose.

3 Methemoglobin producing substances such as sodium nitrite, amyl nitrite, methylene blue, toluidine blue, pyrogallol, procatechin, phenylhydrazine, and potassium ferrocyanide.

In group one only sodium tetrathyocyanate was strong enough of itself to be of much use, and it was so toxic as to preclude its use. Sodium thiosulphate changes cyanide to non-toxic sulphocyanate, but its value is limited because it has to be given either before or at the same time the cyanide is given.

Of group two, triose—glycerinic aldehyde—was selected for experimentation. It unites with cyanide to form non-toxic cyanhydrine. Very large dosage was necessary and its use further limited by its toxicity which consisted of excitation of the higher nerve centers to produce restlessness, irregular respiration and convulsions.

In group three, the methemoglobin-producing substances, Hug found sodium nitrite to be most effective, that is, smaller doses proved adequate. Amyl nitrite and methylene blue were also effective, and will be considered later.

Both Hug and Wendel pointed out the limitation of the methemoglobin-producing substances. Their antidotal action depends upon the conversion of oxygen carrying hemoglobin into non-functional methemoglobin and then cyanmethemoglobin. Hence their value depends upon the maximal quantity of hemoglobin changeable to methemoglobin without killing the animal from the anoxemia. 40 mg. of sodium nitrite per kilogram is the largest dose that can be given to dogs without killing them. This amount of sodium nitrite will protect a dog from about 4 lethal doses, and it changes about 60% of the total hemoglobin to methemoglobin. This is the top limit of hemoglobin which can be spared without leading to death from insufficient oxygen transport. These same figures hold approximately for men. Furthermore, sodium nitrite is about twice as efficient as methylene blue, and amyl nitrite about one-third more effective than methylene blue.

Analyzing Geiger's first case, which absorbed practically 1 gm. of cyanide, enough methylene blue had to be given to inactivate 1.6 litres of blood, or about one-fourth of the total blood and hemoglobin. This loss of oxygen carrying capacity is not serious. The absorption of 3 gms. of cyanide would require methemoglobin formed from about three-fourths of the total blood volume, or more than 60% of the total, which is the upper limit. Hence, in an average adult, the absorption of much more than 2 gm. of

cyanide will be fatal anyhow, if not from the poison itself, then from the treatment.

Methylene blue is probably not quite so toxic as this reasoning could lead us to suppose. Hanzlik and Richardson,[23] in a recent paper, point out that methylene blue is excreted in the urine in a partially oxidized state, thus restoring the hemoglobin of the blood to its oxygen carrying capacity. When 10 mg. per kilogram of body weight of methylene blue were injected (a dose roughly corresponding to 50 cc. of a 1% solution for an adult) the oxygen carrying capacity of the blood was reduced 11.9% in 10 minutes. After 1 hour, the oxygen carrying capacity was 6.1%, or over half of the dye had been eliminated. Thus, if we give a maximal dose of methylene blue without relief of symptoms, we may repeat at least part of it after one-half to one hour. Moreover, Hanzlik and Richardson remind us that cyanide poisoning is not usually so rapidly fatal as we are wont to suppose, but that a state of coma with convulsions, untreated, may last for two or three hours. This makes it possible for us to give perhaps twice as much methylene blue as if we had to give it all at once.

Hug recommends the slow injection of a 2% solution of sodium nitrite, not to exceed 50 cc. (1 gm. of the drug) for an adult. If further protection is needed he advises the use of the 10 cc. of 3% sodium thiosulphate intravenously in addition to the sodium nitrite, the sodium thiosulphate being of some value by changing the cyanide to an insoluble sulphocyanate, and not forming further methemoglobin. It also seems to act as a synergist and increase the action of the sodium nitrite.

If amyl nitrite is used, by inhalation instead of sodium nitrite intravenously, Chen, Rose, and Clownes[21] recommend inhaling a 0.3 cc. pearl every 15-30 minutes until the patient has recovered. If breathing ceases artificial respiration should be instituted and the amyl nitrite continued. The pulse and respiration should be watched for 24 hours.

Hanzlik and Richardson[23] point out that the nitrites, especially sodium nitrite, are extremely dangerous to use, because of the possibility of the well-known nitrite reaction, leading to circulatory collapse. When we notice that from 0.7 gm. to 1.4 gm. of sodium nitrite must be given intravenously, we realize the danger of inducing circulatory collapse, even with small divided doses. Hence, methylene blue seems to be the safest of the methemoglobin forming antidotes, although less efficient as an antidote than the more toxic sodium nitrite.

Hanzlik and Richardson recommend the intravenous injection of 50 cc. of 1% methylene blue which may be repeated up to a total of 200 cc. to 300 cc. for an adult. A 1% aqueous solution of methylene blue may be used, or preferably a 1% solution in 1.8% (isotonic) sodium sulphate, which makes a very stable solution. Gastric lavage should be performed promptly with 5% sodium thiosulphate. Artificial respiration, administration of oxygen-carbon dioxide mixtures and circulatory stimulants such as caffein and adrenalin should be used as indicated symptomatically.

It is now apparently firmly established that the methemoglobin-producing substances are excellent but limited antidotes for cyanide poisoning. They act by producing a substance, methemoglobin, which forms insoluble, non-toxic compound, cyanmethemoglobin, from the cyanide, and not by replacing the oxidizing ferments of the tissues. Methylene blue appears to be the most satisfactory of these methemoglobin-producing substances.

What is the value of methylene blue in carbon monoxide poisoning? To recollect, Geiger and several others have reported favorable results with methylene blue in cases which received also the customary oxygen, carbon dioxide and artificial respiration when necessary. How does carbon monoxide cause death? Cyanide, as Warburg pointed out, kills by inactivating the oxidizing ferment of the tissues. Warburg also showed that carbon monoxide combines with these tissue ferments, inhibiting their activity as does cyanide. In bloodless tissues, a concentration of 95% carbon monoxide (and 5% oxygen) is necessary to even partially inhibit the respiratory ferment of the tissues. A mixture of .1% carbon monoxide (and 21% oxygen) is fatal to man. In other words, the affinity of the hemoglobin of the blood for carbon monoxide is several thousand times greater than the affinity of the tissue ferments for carbon monoxide, and long before the tissue ferments have received enough carbon monoxide to inactivate them the hemoglobin is completely saturated with carbon monoxide. Thus, death in carbon monoxide poisoning is due to asphyxia from the replacement of oxygen carrying hemoglobin with carbon monoxide hemoglobin.

Now, Haggard and Greenburg[22] remind us that methylene blue is successful in cyanide poisoning

because it produces methemoglobin, and not by stimulating tissue respiration of itself. When given for carbon monoxide poisoning it also produces methemoglobin. Methemoglobin does not carry oxygen, in fact, when sufficient methemoglobin has been produced (from two-thirds of the total hemoglobin), the patient dies from asphyxia. To give methylene blue to a patient with carbon monoxide poisoning is to decrease further the hemoglobin for oxygen transport already limited by carbon monoxide, and therefore to increase the anoxemia. Theoretically, at least, methylene blue is synergistic with carbon monoxide and definitely contraindicated in carbon monoxide poisoning.

Haggard and Greenburg show that the carbon monoxide content of the blood falls 20-30% in 15 minutes after a person is removed from the poisonous atmosphere. In all the cases reported as successfully treated with methylene blue, at least one-half hour to an hour and a half had elapsed before the dye was given. Hence these patients had excreted enough carbon monoxide so that the administration of methylene blue was not fatal, but it could not have been beneficial. The counter shock caused by the pricking with the intravenous needle would probably have been sufficient to waken them.

M. M. Brooks,[11] who cited experiments to show the value of methylene blue in carbon monoxide poisoning, did not inject the controls with even saline solution. Haggard and Greenburg repeated her experiments, using both rats and dogs. Groups of both animals were gassed to almost cessation of respiration, then half were given intravenous methylene blue (10 mg. per kilogram) and half saline. The results indicated that the saline controls were able to walk when they still had 48% carbon monoxide in their blood and only 52% free hemoglobin for oxygen carrying. The dogs with methylene blue did not walk until their blood carbon monoxide was down to 28% (as compared with 48% of the controls), and their free hemoglobin was 63% (as compared with 52% of the controls). They had in addition 9% methemoglobin from the methylene blue. The most striking results, however, were not apparent until the second day, when the animals who had received methylene blue appeared ill, lethargic and had shaking legs upon standing, while controls were normally active.

Haggard and Greenburg thus strikingly prove both theoretically and experimentally that methylene blue is of no value, and is even harmful in cases of carbon monoxide poisoning. It is interesting to observe that since their discussion, published last June, no one has reported a case of carbon monoxide poisoning, treated with methylene blue, nor has anyone tried to demonstrate its value experimentally.

By way of summary we might make the following conclusions:

1. Cyanide causes death by inactivating the oxidative ferments of the tissues. Methylene blue forms methemoglobin with the hemoglobin of the blood. This forms an insoluble, inactive compound with cyanide, cyanmethemoglobin, and is an effective antidote for up to 3 gm. of the poison in an adult. The various techniques of treatment, in order of preference, are as follows:

(a) Intravenous injection of 50 cc. of 1% methylene blue which may be repeated up to a total of 200 cc. for an adult (300 cc. over a period of one or two hours).

Prompt gastric lavage with 5% sodium thiosulphate.

Administration of artificial respiration, oxygen-carbon dioxide mixtures, and circulatory stimulants such as caffein and adrenalin, as indicated symptomatically.

(b) Intravenous sodium nitrite, 50 cc. of a 2% solution (1 gm.), given preferably in 5 doses of 10 cc. each during 1 hour and with adrenalin ready to combat circulatory collapse.

Intravenous sodium thiosulphate, 10 cc. of a 3% solution as a synergist to the sodium nitrite.

Use of gastric lavage, respiratory and circulatory stimulants as above in (a).

(c) Inhalation of amyl nitrite pearls (.3 cc. each) every 15-30 minutes until recovery.

Use of gastric lavage, respiratory and circulatory stimulants as in (a).

2. Methylene blue and its allied drugs have no use, either theoretically or experimentally, as antidotes for carbon monoxide poisoning. They are, in fact, definitely contraindicated. Our treatment of carbon monoxide poisoning is still the use of oxygen and carbon dioxide, artificial respiration when necessary, and the use of cardiac and respiratory stimulants.

A pertinent question that no one has considered is "after the cyanide has been detoxified by the methemoglobin, what becomes of the cyanmethemoglobin which has been formed?"

BIBLIOGRAPHY

1. J. C. Geiger: J. A. M. A. 99:1944; Dec 3, 1932.
2. J. J. Hanzlik: J. A. M. A. 100:357; Feb. 4, 1933.
3. Sahlin: Scandinav. Arch of Physiol. 47:284; 1926.
4. Eddy: J. Pharmacol. and Exp. Therap. 39:271; 1930.
5. Eddy: J. Pharmacol. and Exp. Therap. 41:449; 1931.
6. M. M. Brooks: Proc. Soc. Exper. Biol. and Med. 29:1228; 1932.
7. M. M. Brooks: Am. J. Physiol. 102:145, 1932.
8. O. W. Warburg: Die Naturwissenscaften 20:26; 1928.
9. J. C. Geiger: J. A. M. A. 101:269; July 1933.
10. J. C. Geiger: J. A. M. A. 100:1103; April 1933.
11. M. M. Brooks: Am. J. Physiol. 104; April 1933.
12. A. W. Christopherson: J. A. M. A. 100:2008; June 1933.
13. Jallhass: J. A. M. A. 100:1862; June 1933.
14. M. A. Bell: J. A. M. A. 100:1402; May 1933.
15. Compemale: Comp. rend. Soc. de Bio 43:300; 1891.
16. Wendel: Proc. Soc. Exp. Biol. and Med. 27:624; April 1930.
17. Wendel and Schaffer J.: Biol. Chem. 87:XX; June 1930.
18. Warburg: Kubowitz Christian Bio. Chem. Ztschr. 222:245; 1930.
19. Wendel: J. A. M. A. 100:1054; April 1933.
20. Hug: J. A. M. A. 100:1621; May 1933.
21. Chen: Rose-Clownes J. A. M. A. 100:1920; June 1933.
22. Haggard and Greenberg: J. A. M. A. 100:2001; June 1933.
23. Hanzlik and Richardson: J. A. M. A. 102:1740; May 1934.

PERNICIOUS VOMITING OF PREGNANCY

By DR. FRANK S. HALE
253 ELMWOOD AVENUE, PROVIDENCE, R. I.

There are few medical problems that have produced such a variety of opinions or such an array of weird remedies as hypermesis gravidarum. It has been labeled as an obsession, a non-entity, and more charitably, as a simple neurosis. Its essential cause still is unknown. Many "miracle men," as DeLee calls them, have proposed methods of treatment or medication, the general use of which has always been disappointing. With our present understanding, or more exactly, our actual lack of knowledge of the essential cause, supportive treatment, combined by a most thorough ruling out of the presence of any other contingent disease, seems to be the most satisfactory treatment for pernicious vomiting.

That a woman be pregnant, does not give her immunity to incurrent diseases that in themselves may produce severe vomiting. Examples of such conditions are: gastric ulcer, gall bladder disturbance, abdominal cancer, tubercular peritonitis, brain tumor, and acute appendicitis. I shall not describe here the technique required to eliminate the possibility of these conditions, but occasionally, autopsy does show such pathology in a death which has been attributed to hypermesis gravidarum.

Negligence in treatment of the usual vomiting of pregnancy may so dehydrate the patient as to transfer her to the pernicious type. Experimentation should have no place in the severe cases, and even simple morning sickness is quite definitely helped by some degree of routine supportive care.

Whatever the essential cause may be, four factors stand out in varying degrees in these cases, namely:

1—Dehydration. 2—Starvation. 3—Disturbance of the hepatic balance. 4—Neurosis.

Hospitalization, of course, in all severe cases is to be recommended.

The neurosis is treated by rest, isolation, and sedatives. Bromides or small quantities of chloral by rectum are most commonly used. I am quite partial to Dial "Ciba" as this may be given hypodermically.

The dehydration and much of the starvation may be cared for by intermittent saline glucose or dextrous 10-25%, 200-300 cc. once to three times a day, and in severe cases, continuous venaclysis is given 3,000 cc. daily of a 5-10% saline glucose or dextrous solution. Some cases showing slow improvement may require the addition of protein caloric support—especially if urobilinuria is persistently present. This, of course, indicates hepatic derangement. Such protein nourishment as white of egg, milk, etc., may be given through a duodenal tube. The indications of improvement are: (1) Increased urinary output in two or three days up to 1,000 cc. with a 1.010 specific gravity. (2) Cessation of vomiting should occur within 72 hours. Food should then be taken by mouth in small quantities at frequent intervals, the type diet seeming to be immaterial. (3) Retention, followed by a gradual gain in weight. I would say here that too early discharge from the hospital is a mistake, as relapses too often occur.

Unsatisfactory progress is noted by:

1. Persistently concentrated and meager urinary output.

2. Urobilinuria constantly in the urine.
3. Presence of jaundice probably denoting acute yellow atrophy of the liver.
4. Continual vomiting in spite of gastric rest.
5. Progressive loss of weight and weakness.

In the classic presentation of hypermesis, which we have all read, given in 1852 by Paul Debois at the French Academy of Medicine, he divided, for easier description, the disease into three progressive stages. A patient should never be permitted to reach the final harrowing terminal stage of delirium, somnolence, stupor and coma. Interference then is futile. During all this disturbance, the foetus usually remains alive. Occasionally, however, it does die, vomiting then stops, and spontaneous abortion occurs.

Termination of pregnancy even with an intensive supportive treatment may be very rarely required. This is a most delicate point. Consultation then to verify diagnosis, share the responsibility, and to avoid any question of undue haste or illegality, is most desirable.

Intravenous saline glucose therapy has come into such everyday use that we tend to forget the extensive and continued study along this line by Hendon, Matas, and especially Paul Titus of Pittsburgh. It is through the courtesy of one of the latter's co-workers, Dr. Eiselman, together with my observations at the Elizabeth Magee and St. Margaret's clinics, and my service and private practice, that this subject matter is derived.

The remarkable improvement of a dehydrated patient after intravenous saline glucose, is quite comparable to a blood transfusion in hemorrhage cases, 200-300 cc. of a 25% solution given t.i.d., represents considerable actual sustenance — roughly, 6 oz. of glucose or dextrous. In the continuous veneclysis method, up to 3,000 cc. daily of a 10% solution does not embarrass the circulation, is not uncomfortable for the patient, and may be continued for a week or more. This treatment is equally efficacious in the post-operative treatment of gastric and intestinal cases. Special apparatus is necessary for veneclysis, and carefully prepared, pure solutions prevent reactions. A recent change in this therapy is the addition of calcium gluconate, which may be given intramuscularly. Clysis has so many advantages over rectal fluids that the rectum is used only for medication and cleansing enemas. Insulin is seldom needed to counteract the varying amounts of glucose. Before leaving the subject of this phase of the treatment, I may add that it is our experience at St. Joseph's that Titus' method of estimating liver damage by the rapidity of glucose absorption (as shown by repeated blood sugars) is of excellent prognostic value. Obviously, then, saline glucose either used intermittently or as continuous venoclysis, is the most important factor in our present supportive treatment for all of the severer cases of the vomiting of pregnancy. Hospitalization is necessary for this type, and many cases will require special duty nursing.

No paper seems complete without some statistics. I quote here from the Maternal Death Report, United States Department of Labor—"Although pernicious vomiting of pregnancy was the primary cause of death given for only 61 of the 7,380 women included in the study, it was a contributing factor in 191 other cases. The duration of the vomiting before the physician was called was given in 164 of the 252 cases. It had lasted less than a week in 49 cases, from 1-2 weeks in 24 cases, from 2-4 weeks in 28 cases, and 4 weeks or longer in 63 cases." It goes on—"The condition that 227 of these 252 women were in when they were first seen by the physician was noted. Twenty-nine were said to have been in good condition, 62 in fair condition, 136 in poor condition." The following comment is given by the Advisory Committee: "The chief method of attack against the severe toxemias of pregnancy is conceded to be their early detection and control. For this it is necessary to have continuous intelligent medical supervision of the prospective mother from early in pregnancy. Evidently there is a great need for education of patients and families."

Conclusions

1. The purpose of this paper is to stimulate an interest in early adequate treatment of the ordinary vomiting of pregnancy. It is neither a non-entity nor a simple neurosis. The patient is ill and needs and deserves rest and care.

2. Other conditions besides the pregnancy may be causing the vomiting. Such possibilities should be thoroughly investigated.

3. Briefly, to outline an intensive supportive treatment which in most cases will sustain the patient until she has overcome her toxicity.

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EDITORIALS

MEDICAL UNEMPLOYMENT RELIEF

The plan of the Rhode Island Medical Society for medical care of the unemployed and their families was published in the October number of this JOURNAL. This plan seems to us to be a good one. These people must be taken care of and there are too many of them to be cared for properly on a charity basis by private physicians. This is true especially as the greater number of them call on the physicians who practice chiefly among the poor and who cannot afford to spend the greater part of their time on charity work. Some of these physicians are doing a large practice without being paid enough to live on.

This plan also conforms very closely to the ten principles to be followed in social experiments as recommended by the A.M.A. Although the medical profession does not absolutely control the administration of the plan, the committees of physicians have considerable influence and in those communities where the committee has been active the medical profession has been able to guide the administration.

A very few physicians are trying to make as much money as they can without reference to the

needs of their patients for treatment and it is the duty of the committee of the local medical society to prevent this. In Providence the committee inspects the bills. This would seem to be important in order that the ninety-nine physicians who are acting in good faith should not suffer in reputation on account of the one who visits his patients frequently in order to run up a large bill at the taxpayers' expense.

There are other problems which need different solutions in different localities, such as the question of prescriptions and how they shall be filled, and what care shall be given chronic invalids and those who need special treatments and appliances. All these questions must be decided by conferences between the committee of physicians and the Emergency Relief Administrator.

We believe that if the local medical societies through their committees will give sufficient attention to the details of this plan that it will be of great benefit to both the unemployed and the physician.

GERIATRICS AND SURGERY

How many aged people are allowed to die when a surgical operation, performed by skilled hands, might prolong life and make them comfortable enough to enjoy it?

There are many women past 80 years of age who could and would undergo a gall bladder operation if the physician were optimistic. We are often inclined to be unduly pessimistic in dealing with patients of advanced years. The problems of senility are interesting.

Aged diabetics may successfully undergo operation in skilful hands and under ethylene anesthesia. We do not hesitate to operate on aged diabetics. There are many old women to whom life has become a nightmare because of cholecystitis or prolapsus uteri. Of course, it would be better to correct those abnormalities at the age of 50 or 60, but there is no reason why persons past 80 or 90 should not be given a chance to live a little longer and comfortably.

Take for instance the old man who suffers from cholelithiasis, the question of cancer or cirrhosis of the liver enters into the picture. The Takata-Ara reaction may rule out advanced cirrhosis, but only exploration will elicit the presence of carcinoma. It is advisable to give old people a chance and operate; to consider them doomed is a mistake, unless they happen to be abnormally weak.

Advanced years are not always a handicap on the operating table. They often stand operative shock far better than younger patients. It is amazing to see a man of 85 undergo an operation for peptic ulcer and rally. A most able surgeon and equally able anesthetist are necessities in such cases—a surgeon who is not only deft but quick and will work with a minimum of injury and manipulation of the tissues. Several years ago that famous surgeon, Robert T. Morris, advocated that in the fourth era of surgery we would operate with a minimum of manipulation of the tissues and with a very small incision. He was a good prophet.

Preparing the senile patient for operation is essential: intravenous saline the night before is often satisfactory, intravenous glucose on the morning after operation, and subcutaneous glucose and saline at night, this repeated every day until the intake and retention of fluids are satisfactory. This often gives excellent results. The senile patient should be out of bed soon after operation, if his condition warrants it. Some surgeons get their old patients out of bed on the third day and home on the seventh day following appendectomy. There is a tendency to keep old people in bed too long. This is a misconception of the factors involved; obviously less danger of embolism or pneumonia if the patient gets up soon after operation.

Give old patients the chance to rally and enjoy life as long as possible. The results of our efforts will often surprise us.

PUBLIC HEALTH AND PRIVATE PRACTICE—THE DETROIT PLAN.

Studies of the costs of medical care have suggested that the socialization of medicine, though resisted by the profession in the hope that nothing may interfere with the ideal status of the family physician, nevertheless may be in the end the inevitable result of various disruptive economic forces now at work. The multiplication of health agencies with the introduction into various communities of clinics staffed by a salaried medical personnel without the advice or consent of the local medical profession is socialization of a thoroughly bad type and, as the JOURNAL has recently pointed out, open to great criticism. Under such circum-

stances the agencies of public health and private practice stand opposed—where understanding and co-operation are most needed—in as much as the prime object of both is the health of the citizens of the state.

In this connection a consideration of the "Detroit Plan" so ably presented by Dr. Henry F. Vaughn at the recent meeting of the Providence Medical Association is most appropriate. Professional participation in health work is the essence of the plan. It involves abolition of many of the free clinics with a return of the patient to the family physician for the work that the clinic previously had performed.

Described briefly the "Detroit Plan," sponsored by the Wayne County Medical Society, including the city of Detroit and three rural counties, consists of a training of the medical profession to carry out public health procedures, beginning with diphtheria immunization, abolition of free clinics for this work, an educational campaign by public health nurses, the sending of the patients to offices of the private practitioners who have agreed to hold a definite office hour for this work and a fixed minimum fee for the procedure with compensation from public funds where the patient is unable to pay. The whole plan has been developed and is administered by the local medical society and the board of health jointly.

Such a plan of co-operation has many obvious advantages not the least of which is the definite return of the patient to the office of the family doctor where he belongs. It not only eliminates the interference with private practice of which the free clinic has at times been guilty, but it increases public respect for the family doctor as an exponent of preventive as well as curative medicine and constitutes him officially a deputy health officer and an integral part of the public health organization. Financially, the doctor does not lose. In the actual application of this plan in Detroit in the matter of diphtheria prevention, it is estimated that five times as much money has been paid to the doctors of the city as they could have collected for the care of the illness which would normally have occurred had the program not been in force.

It must be admitted that the cost of operating the plan is somewhat greater than that of mass immunization by paid workers in free clinics. It is the general opinion, however, that the greater amount of actual protection of the public which is achieved, the improvement in the training and in the status of the family physician in his relation to the public and to the public health authorities repays the extra cost many times over.

In this matter the first move is up to the local medical societies. In Charleston, W. Virginia, St. Louis, Mo., Albany, N. Y., and elsewhere modifications of the plan are being attempted and early reports indicate success. The JOURNAL respectfully suggests that here also, preferably in Providence where leadership in matters of public health can be taken for granted and the District Nursing organization is second to none, the matter be seriously considered. A study of the situation by a committee including representatives of the Department of Public Health will result in a report which will prove of the greatest personal interest to every practicing physician in Rhode Island.

THE NURSING INSTITUTE

The fifth annual Nursing Institute under the joint auspices of the R. I. League of Nursing Education, the R. I. State Nurses' Association and the R. I. State Organization for Public Health Nursing was held at the Biltmore Hotel, November 7 and 8 with a total registration of over seven hundred.

At the first session Wednesday afternoon, sectional meetings were held. Miss Ella Best, R.N., acting Associate Director of the American Nurses' Association Headquarters, spoke at the Private Duty Section on the recent survey of the nursing situation in Rhode Island. In her talk she spoke favorably of the eight-hour day now being instituted in the hospitals of neighboring states.

At the Institutional Section, Miss Helen Wood, Director of the School of Nursing at Simmons College, spoke on the correlation of classroom teaching with ward practice. Miss Harriet Frost, Director of Public Health Nursing at the New York Hospital, spoke to the Public Health Nurses on the need of adequate health teaching along with the home nursing care.

At the dinner meeting, Miss Jane Louise Mesick, Dean of Simmons College, gave suggestions how professional people may use their leisure time for greater stimulation and enjoyment.

At the evening session with Miss Mary Sewall Gardner presiding, Miss Sophie C. Nelson, recently president of the National Organization for Public

Health Nursing, spoke on "Every Nurse a Health Teacher." She emphasized the fact that the public is interested only in the results we obtain and not in our problems. In her talk she referred several times to the many contributions made by Dr. Charles V. Chapin to the field of Public Health.

At the Thursday afternoon session, an excellent symposium on Diseases of the Thyroid was presented by a group of the doctors representing the Homeopathic Hospital. Dr. Frank E. McEvoy gave the general talk and was followed by Dr. James H. Fagan, who presented some typical cases, and Dr. Russell Hunt, who discussed the X-ray interpretations. The nursing care was discussed by Miss Martha Peckham and Miss Edna Rydberg.

At the Thursday dinner meeting, Mr. Page Potter gave those present some useful advice on how to arrange and care for flowers, urging nurses to be "flower conscious."

The Thursday evening session, at which Dr. James Gordon Gilkey spoke on "The Secret of Getting a Lot Done," was well attended and of great interest to those present. He emphasized the point that everyone could accomplish more if they would use their time to good advantage and would overcome their personal conflicts.

An interesting side line of the Institute was the Hobby Show at which many of the nurses displayed work or interests carried on in their leisure time.

QUINIDIN SULPHATE THERAPY

By CLIFTON B. LEECH, M.D.
211 ANGELL STREET, PROVIDENCE, R. I.

Quinidin sulphate is a drug which has a definite although somewhat limited field of usefulness, chiefly in the treatment of disorders of the mechanism of the heart beat. Its mode of action, toxic effects, contra-indications and therapeutic value have become sufficiently well elucidated during the past fifteen years to permit of a brief survey of the subject.

Physiologic Action

The chief effect of the drug is to lengthen the refractory time of the heart muscle, especially in the auricle, which tends to abolish the circus movement responsible for many of the paroxysmal disorders of the heart beat. Speed of auricular conduction may also be slowed, in antagonism to the breaking up of the circus movement, but the former is usually the predominating effect. A third action is that of depression of the vagi nerves, but this is usually not marked and seldom produces more than a temporary acceleration of the ventricular rate. Quinidin may also depress auriculo-ventricular conduction by a direct action upon the conduction tissues though this rarely plays an important part in the therapeutic action of the drug. The effects of quinidin are dependent upon the amount of the drug given within a short period rather than upon an accumulation within the body as a result of smaller amounts administered during a longer time.

Toxic Effects

The toxic effects are chiefly those of ordinary cinchonism—headache, dizziness, deafness, tinnitus, nausea, vomiting, urticaria and diarrhoea. There may occur a very rapid, regular heart action at a rate higher than before administration of the drug; rarely, intraventricular block may develop. When frequest doses are given, observation of the patient should be made for toxic effects before each new dose, and therapy discontinued if such signs develop. Usually large doses are well tolerated. Occasionally idiosyncrasy is met with. In order to avoid harming an individual sensitive to the drug, it is customary to give by mouth a test dose of 1½ to 3 grains before beginning the therapy proper. A very rare toxic effect is that of cardiac standstill: such an event probably would be preceded by other warning signs of toxicity.

Contra-indications

Aside from idiosyncrasy, the drug is contra-indicated in patients who have or have had auricular fibrillation with circulatory stasis as shown by hæmoptysis, venous engorgement or edema, or who present great cardiac enlargement. In such patients the favorable action of quinidin in restoring regular rhythm may bring about embolism by throwing into the circulation bits of intracardiac thrombus. Of course, any heart which contains a thrombus, as do many auricles in the case of persistent fibrillation of the auricles, is likely at any time to pump out an embolus. In this connection I was once told by Dr. E. P. Carter of the Johns Hopkins Hospital that in a series of patients with auricular fibrillation from whom he withheld quinidin there occurred six sudden deaths, presumably due to embolism. However, if we administer quinidin to such patients and they die suddenly we wonder what the drug had to do with it. It seems better to avoid any action which tends to increase the likelihood of embolism.

Premature Beats

While quinidin has been recommended for the treatment of premature beats and extrasystoles of both auricular and ventricular origin, in actual practice such therapy is not often successful. I have been so frequently disappointed in this respect that I now use quinidin for this purpose only when other measures have failed.

Paroxysmal Auricular Tachycardia

Paroxysms of auricular tachycardia, of sudden onset, usually terminate spontaneously within a few minutes to a few hours. Quinidin does not act rapidly enough to be of special use in the treatment of the acute attack unless it be greatly prolonged, in which case the drug may be of great service. For example: on April 1st, 1934, I saw, with Dr. Samuel Adelson of Newport, a man of forty-eight years who had had within a three-year period, three attacks of paroxysmal rapid heart action. One attack lasted two weeks, another two days, the third one and one-half days. At the time of my visit he had been in bed for thirteen days during which entire time his pulse rate had been 180. The onset had been sudden, following no particular exertion or other evident cause. The patient was conscious of the tachycardia, which was uncomfortable but painless, and felt very weak. He had been kept awake by the incessant feeling of palpitation. Physical examination revealed no definite evidence of cardiac enlargement. The tachycardia made it impossible to ascertain with certainty about the presence of cardiac murmurs, but none were heard. The heart sounds were moderately poor in quality. The rhythm was absolutely regular, rate 180. There were signs of circulatory congestion in the liver and lungs. The blood pressure levels were 150 systolic, 90 diastolic. Various types of vagal stimulation failed to effect the rate or rhythm of the heart. There was no change in the heart rate following change of posture from reclining to upright. The patient had had digitalis, and earlier in the attack had been given six three-grain capsules of quinidin sulphate at three-hour intervals. It seemed obvious that circulatory failure had begun and was likely to increase if the rapid rate continued much longer. It was decided to administer by mouth three grains of quinidin sulphate every hour until the heart rate changed or toxic signs appeared. After eighteen such doses the heart rate dropped to 140. Quinidin was then omitted. A few hours later the rate was 80. The next day the rate was 50 and remained so for about ten days, when it gradually increased to its present level of 70 to 78.

While quinidin is not very often needed in the treatment of acute attacks of paroxysmal auricular tachycardia, it is of considerable value in the prevention of such attacks in the case of individuals who are subject to frequent paroxysms. In my experience quinidin never fails to prevent to some degree the occurrence of these attacks. Usually the dosage can be so regulated as to prevent their occurrence almost entirely. The proper dosage is a matter of trial in each individual. I usually begin with three grains three times a day, lessening the frequency of the dose as time passes without the appearance of the tachycardia. Usually a ration of three to six grains per day is sufficient to either abolish the paroxysms or to make them so infrequent and of such short duration as to be of little consequence.

Paroxysmal Ventricular Tachycardia

This type of tachycardia is rare and seldom occurs except as evidence of a serious disturbance of the myocardium. Treatment of the acute attack must take into consideration the underlying cardiac pathology, but in the case of a persistent ventricular tachycardia quinidin may be used in a manner similar to that described above. Occasionally the results are dramatically satisfactory, but in general are not so reliable as in the treatment of auricular tachycardia.

Paroxysmal Auricular Fibrillation

Patients with paroxysmal auricular fibrillation, who have no signs of circulatory failure, especially in the absence of valvular disease, are particularly suitable for quinidin therapy since about two-thirds of them may thereby be restored to normal rhythm, many of them to maintain the normal mechanism even without quinidin rations. It goes without saying that possible causes of this disturbance, such as hyperthyroidism, should be searched for and eliminated. The precise dose and frequency of dose is a matter of individual opinion and experience. The drug may be given by vein, but it seems safer and better to use the oral route. Since it seems to be established that the effectiveness of the remedy is dependent upon the total amount in the body at a given time rather than upon the total amount administered over a period of days, I prefer to give, as previously indicated, three grains every hour until some sort of effect is produced. I do not

always interrupt sleep for this purpose. When normal rhythm occurs the drug is omitted. If the auricular fibrillation recurs and normal rhythm is again restored by quinidin, I then give daily rations in an attempt to prevent further recurrences of the arrhythmia. Sometimes it is impossible to succeed in this except by such large daily doses as to produce the unpleasant effects of cinchonism.

Established or Chronic Auricular Fibrillation

Patients with persistent auricular fibrillation often present contra-indications to quinidin and many others are so well controlled by digitalis that it seems unnecessary to attempt to restore regular rhythm. I have seen patients who were more comfortable when fibrillating with a slow ventricular rate, then when regular with a more rapid and less easily controlled ventricular rate. When no contra-indications exist and it seems desirable to restore normal rhythm by quinidin, the method is similar to that in the case of paroxysmal auricular fibrillation. It should be added that during such radical quinidin therapy, in all cases, the patient should be kept in bed.

Paroxysmal Auricular Flutter

This type of rapid rhythm often accompanies true myocardial disease and is apt to last longer than the ordinary attack of paroxysmal auricular tachycardia, and is often very difficult to abolish or control. Frequently it is successfully treated by digitalis, which often throws the rhythm into auricular fibrillation which in turn may spontaneously revert to normal rhythm, or, failing that, can be controlled by digitalis. Occasionally, however, quinidin is of the greatest value in the treatment of otherwise intractable instances of auricular flutter. Following is an example of this: a healthy laborer of thirty-five years, with a completely negative previous history, was placing a heavy cake of ice in a refrigerator one day last August when he suddenly felt a sensation as of a "twist" in his chest, followed by feelings of weakness and faintness. He went home to bed and the next day he felt pain in his abdomen, was nauseated and vomited several times. The same day he was admitted to a hospital where his pulse was found to be very rapid and weak, his blood pressure seemed to be about 70 systolic, the abdomen was tender with a smooth liver edge palpable about three fingers' breadth below the costal margin. No other important findings. The man felt very weak and drowsy. During the next three days he received 4.2 grammes of digitalis without effect on the heart rate or rhythm. At the end of the third hospital day I saw the patient and found a regular heart rhythm, rate 132, synchronous with visible pulsations in the carotid vessels which were overlaid by extremely rapid venous pulsations. I found the blood pressure to be 100 systolic, 60 diastolic. The man was stuporous, hard to arouse, would not eat, took very little fluids, but showed no evidence of circulatory failure except the enlarged liver. The heart seemed slightly enlarged, but no definite evidence of valvular disease was detected. I advised quinidin sulphate by mouth, three grains each hour for six doses, then three grains every two hours until the rhythm or rate changed or toxic signs appeared. During the next forty hours he received eighty-one grains of quinidin, at which time the rate suddenly dropped to 88. Examination by me one week later revealed no signs of heart disease, or of circulatory congestion in the liver. The patient returned to work as a truck driver shortly after and was reported last week as feeling well. I think this was a case of auricular flutter of sudden onset, as a result of physical exertion, occurring in a normal heart, terminated by quinidin therapy.

In patients who are subject to attacks of auricular flutter, daily rations of quinidin are sometimes effective in reducing the duration and number of such attacks.

Prevention of Ventricular Fibrillation

Fibrillation of the ventricles causes death if it persists for longer than a few seconds. It is said to be the cause of death in a small percentage of cases of coronary thrombosis. It has been suggested that quinidin might be administered routinely to patients with recent coronary occlusion as a possible preventive of ventricular fibrillation. I have had no experience with such a procedure and know of no statistics in regard to it.

Conclusion

Quinidin sulphate is useful in the treatment and prevention of nearly all of the various types of cardiac arrhythmia. When used with a clear understanding of its mode of action and its dangers, it can be given in much larger dosage than is generally used. In the treatment of acute attacks of arrhythmia it is well to remember that since quinidin is rapidly excreted the amount given in a day or so is much more important than the total amount given over a long period. The fixed daily ration of quini-

din, used in the prevention of arrhythmia, produces its effects rapidly and, therefore, toxic effects are not likely to result from an accumulation of the drug.

OBITUARY

William F. Flanagan died February 20, 1934. He was born April 28, 1872, and received his early education in the Apponaug grammar schools and La Salle Academy, Providence. He attended Manhattan College, from which he graduated in 1895 with the degrees A.B., A.M. He graduated in 1900 from the Long Island College Hospital.

Dr. Flanagan began practice in 1900; was Visiting Surgeon to St. Joseph's Hospital from 1903 to 1916, and Medical Superintendent of St. Joseph's Hospital from 1916 to 1920.

He was a Fellow of the American College of Surgeons, the Rhode Island Medical Society, the Providence Medical Association, the American Medical Association, and the Society of Military Surgeons of the United States.

Dr. Flanagan was successively Surgeon Major, Lieutenant Colonel of the First Light Infantry of Rhode Island, and retired in 1923 with the rank of Brigadier General.

During his administration as Medical Superintendent of St. Joseph's Hospital, Dr. Flanagan showed overwhelming zeal in his interest in Hospital affairs, and fairness and liberality in the solution of the innumerable problems that devolve upon such a position.

He was most ardent in his religion, and was a profound student of the Latin classics, in which he was highly proficient.

Dr. Flanagan was admired and is mourned by a very large clientele of discriminating patients and by his professional and clerical associates.

JOHN J. KENNEY, M.D.,
W. LOUIS CHAPMAN, M.D.

SOCIETIES

PROVIDENCE MEDICAL ASSOCIATION

The regular monthly meeting of the Providence Medical Association was called to order by the President, Dr. Charles F. Gormly, Monday evening, November 5, 1934, at 8:50 o'clock. The records of the last meeting were read and approved. An invitation to a clinic day at the Memorial Hospital, Pawtucket, on November 7, was read.

The secretary read an obituary on Dr. William F. Flanagan, and Dr. Charles H. Leonard read one on Dr. Eugene P. King. It was voted to spread these on the records and send copies to the families.

The association having voted the president should appoint a committee to consider improvements in the meeting hall, the following were named: James W. Leech, chairman, John G. Walsh, Harry C. Messinger, William Hindle, William P. Buffum, president and secretary ex-officio.

Dr. Francis Chafee moved that a committee of seven be appointed by the president, himself to be a member ex-officio in addition, to investigate the practicability of founding a Donors' Bureau under the auspices of the association, and if they find it to be feasible, to proceed with the establishment of such a bureau. This was voted and the committee was named as follows: B. Earl Clarke, George W. Waterman, Robert H. Whitmarsh, James Hamilton, Kalei Gregory, Jesse P. Eddy, 3rd, Francis H. Chafee, chairman, and the president of the association.

Dr. Kingman for the Public Relations Committee reported on the meeting held Monday, October 8th, and stated that there would be another meeting or meetings later. He then introduced the following motion which was passed: "Moved that the president of the Providence Medical Association appoint for one year a Public Health Clinic Committee of five members, preferably from members practising outside the City of Providence. This committee to co-operate with the Public Health Clinic Committee of the Rhode Island Medical Society."

Dr. Elihu Wing introduced the following resolution: "That the Providence Medical Association, appreciating the increasing number of school teachers showing undue fatigue and nervous states, wishes to call to the attention of the School Committee of the City of Providence this serious situation of the medical and mental health of many of our school teachers and asks that consideration be given towards improving this situation"—and he moved that this resolution be referred to the Public Relations Committee to further study the problem and co-operate in any way that is deemed wise with the proper school officials. Drs. McDonald, Ruggles and Donley endorsed this and it was so voted.

The first address of the evening was by Henry F. Vaughn, Commissioner of Health of Detroit, Michigan, on "The Family Physician and Preventive Medicine." He first paid a fine tribute to Dr. Chapin. He advocated a plan for the medical participation of physicians doing private practice in Public Health Service. To teach him to practice Public Health in his office would benefit the public. This does not mean the elimination of a governmental Public Health Service, for it must be officially supervised. To suggest how this can be developed he outlined the Wayne County Plan. This has to do only with diphtheria, but it serves as an entering wedge. The giving of Schick tests, toxin, antitoxin and other procedures used in the modern methods of combatting diphtheria are all done by practicing physicians for regular fees, the Board of Health remunerating them at reduced fees for cases unable to pay. With slides he outlined the progress of this work and explained their methods of attaining publicity, educating the physicians and allied groups as nurses, social groups, teachers, etc.

Dr. John E. Gordon, Epidemiologist, of the W. K. Kellogg Foundation, spoke on "Newer Aspects in the Control of Communicable Diseases." He has recently traveled through Europe, and he outlined the different diseases as they occurred and as they are handled in the European countries.

Dr. Richardson discussed the papers.

The meeting adjourned at 11:00 P. M. Attendance 189.

Collation followed.

Respectfully submitted,

PETER PINEO CHASE,
Secretary.

ANNOUNCEMENT

Application blanks are now available for space in the Scientific Exhibit at the Atlantic City Session of the American Medical Association, June 10-14, 1935. The Committee on Scientific Exhibit requires that all applicants fill out the regular application form and requests that this be done as early as convenient. Applications close February 25, 1935.

Persons desiring application blanks should address a request to the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago, Illinois.

NOTICE

To insure prompt attention, the readers of this JOURNAL are advised: That matters pertaining to advertising, mailing and accounts should be addressed the Business Manager, Dr. C. W. Skelton, 106 Francis Street, Providence, R. I.

Other matters, books for review, notices, manuscript, letters, reports of meetings, and all affairs of literary nature should be addressed to the Editor, Dr. Frederick N. Brown, 309 Olney Street, Providence, R. I.

THE FIRST THANKSGIVING PROCLAMATION

Few Americans know that the original Presidential Thanksgiving Proclamation was lost for over a hundred years; that it was found at an auction sale in 1921; that it was bought by the Library of Congress for $300.00; and that it now reposes in the archives of that institution—one of the most valuable documents in the world. The Division of Information and Publication of the George Washington Bicentennial Commission, in a statement issued today, relates the story of the lost proclamation.

On September 25, 1789, Elias Boudinot introduced the following resolution in the House of Representatives:

"Resolved, That a joint committee of both Houses be directed to wait upon the President of the United States, to request that he would recommend to the people of the United States a day of public Thanksgiving and prayer, to be observed by acknowledging, with grateful hearts, the many signal favors of Almighty God, especially by affording them an opportunity to establish a Constitution of government for their safety and happiness."

Harmless as this resolution seems, there were objections to it. In reading the Annals of Congress of that period, we find that Representative Aedanus Burke of South Carolina thought we should not mimic Europe "where they made a mere mockery of thanksgiving."

Representative Thomas Tudor Tucker, also of South Carolina, argued that it was not the business of Congress to ask for a national day of Thanksgiving.

"They (the people) may not be inclined to return thanks for a Constitution until they have

experienced that it promotes their safety and happiness."

These objections, however, were overruled; the resolution was passed and sent to the Senate for concurrence. The Senate approved and appointed its committee to wait on the President. The joint committee was made up of Ralph Izard of South Carolina and William S. Johnson of Connecticut, from the Senate; Elias Boudinot of New Jersey, Roger Sherman of Connecticut, and Peter Sylvester of New York, from the House.

Washington complied with the request and on October 3, 1789, issued his proclamation, calling for a National day of Thanksgiving on Thursday, November 26.

And then the document dropped out of sight. It apparently was misplaced or attached to some private papers in the process of moving official records from one city to another when the Capital was changed. However, it happened, the original manuscript was not in the official archives until 1921 when Dr. J. C. Fitpatrick, then Assistant Chief of the Manuscripts Division of the Library of Congress, and now Editor of the forthcoming George Washington Bicentennial Commission series of Washington's Writings, "found" the proclamation. It was at an auction sale being held in the American Art Galleries of New York City. Dr. Fitzpatrick, an expert in Washingtonia, examined the document and found it to be authentic. It was written in long hand by Wm. Jackson, Secretary to President Washington at the time, and was signed in George Washington's bold hand. Dr. Fitzpatrick purchased the document for $300.00 for the Library of Congress, where it is now kept as a treasure. And no amount of money could remove it.

The original Proclamation of Thanksgiving, and, indeed, the first Presidential proclamation ever issued in the United States, reads as follows:

"By the President of the United States of America.

"Whereas it is the duty of all nations to acknowledge the providence of Almighty God, to obey his will, to be grateful for his benefits, and humbly to implore his protection and favor—and Whereas both Houses of Congress have by their joint committee requested me 'to recommend to the People of the United States a day of public thanksgiving and prayer, to be observed by acknowledging with grateful hearts the many signal favors of Almighty God, especially by affording them an opportunity to establish a form of government for their safety and happiness.'

"Now, therefore, I do recommend and assign Thursday, the 26th day of November next, to be devoted by the People of these States to the service of that great and glorious Being who is the beneficent Author of all the good that was, that is, or that will be—That we may then all unite in rendering unto him our sincere and humble thanks—for his kind care and protection of the People of this country previous to their becoming a Nation—for the signal and manifold mercies and the favorable interpositions of his providence, which we experienced in the course and conclusion of the late war—for the great degree of tranquility, union, and plenty, which we have since enjoyed—for the peaceable and rational manner in which we have been enabled to establish constitutions of government for our safety and happiness, and particularly the national One now lately instituted—for the civil and religious liberty with which we are blessed and the means we have of acquiring and diffusing useful knowledge; and in general for all the great and various favors which he hath been pleased to confer upon us.

"And also that we may then unite in most humbly offering our prayers and supplications to the great Lord and Ruler of Nations, and beseech him to pardon our national and other transgressions—to enable us all, whether in public or private stations, to perform our several and relative duties properly and punctually—to render our national government a blessing to all the People by constantly being a Government of wise, just, and constitutional laws, discreetly and faithfully executed and obeyed—to protect and guide all Sovereigns and Nations (especially such as have shown kindness to us) and to bless them with good Government, peace, and concord. To promote the knowledge and practice of true religion and virtue, and the increase of science among them and us—and generally to grant unto all mankind such a degree of temporal prosperity as he alone knows to be best.

"Given under my hand at the City of New York the third day of October in the year of our Lord 1789.

(signed) George Washington"

Celebration of Thanksgiving Day in America can be traced back to the earliest days of the Massachusetts Bay Colony. From there the custom spread to all parts of the United States.